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Research Article

Prognostic value of sarcopenia on survival outcomes in patients undergoing surgical treatment for gastric cancer

Mide kanseri cerrahisi uygulanan hastalarda sarkopeninin sağkalım sonuçları üzerindeki prognostik değeri

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Abstract

Aim: This study aims to assess the predictive impact of sarcopenia on survival in individuals with surgically treated gastric cancer.

Material and Methods: This retrospective analysis examined individuals who underwent surgery for gastric cancer, categorizing them into sarcopenia and non-sarcopenia groups based on skeletal muscle index from abdominal CT images. The study assessed clinicopathological variables, survival, and prognosis differences between the groups.

Results: The median age of the 84 patients was 59 years (range, 24–80); 64.3% were male. For all patients, 67.9% (n = 57) had sarcopenia and 32.1% (n = 27) did not. According to the ROC analysis, the predictive performance of sarcopenia for mortality was statistically significant (AUC = 0.694; p = 0.012). The best cut-off value of 24.97 yielded 75.8% sensitivity and 61.1% specificity. The median follow-up was 48.6 months, and 18 patients (21.4%) died. Sarcopenia patients had a median survival of 32 months (95% CI: 27.4–36.6), while non-sarcopenic patients had 56 months (95% CI: 43.2–68.8). Sarcopenia was an independent survival predictive factor in multivariate Cox regression (HR = 2.46; 95% CI: 1.24–4.87; p = 0.010).

Conclusion: The identification of sarcopenia through CT imaging at the time of diagnosis in patients with gastric cancer is associated with overall survival rates and serves as a prognostic marker for poor prognosis.

Keywords: sarcopenia, gastric cancer, survival

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Öz

Amaç: Bu çalışma, cerrahi olarak tedavi edilen mide kanserli bireylerde sarkopeninin sağkalım üzerindeki öngördürücü etkisini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif analizde, mide kanseri nedeniyle ameliyat edilen bireyler incelenmiş ve abdominal BT görüntülerinden elde edilen iskelet kası indeksine (SMI) göre hastalar sarkopeni olan ve olmayanlar şeklinde gruplandırılmıştır. Gruplar arasındaki klinikopatolojik değişkenler, sağkalım ve prognoz farklılıkları değerlendirilmiştir.

Bulgular: Toplam 84 hastanın medyan yaşı 59 (dağılım: 24-80) olup, hastaların %64,3'ü erkektir. Tüm hastaların %67,9'unda (n = 57) sarkopeni saptanırken, %32,1'inde (n = 27) sarkopeni saptanmamıştır. ROC analizine göre, sarkopeninin mortaliteyi öngördürücü performansı istatistiksel olarak anlamlı bulunmuştur (AUC = 0,694; p = 0,012). En iyi cut-off değeri olan 24,97 değeri; %75,8 duyarlılık ve %61,1 özgüllük sağlamıştır. Medyan takip süresi 48,6 ay olup, 18 hasta (%21,4) hayatını kaybetmiştir. Sarkopenik hastaların medyan sağkalım süresi 32 ay (%95 GA: 27,4–36,6) iken, sarkopenik olmayan hastaların medyan sağkalım süresi 56 ay (%95 GA: 43,2–68,8) olarak saptanmıştır. Çok değişkenli Cox regresyon analizinde sarkopeni, bağımsız bir sağkalım öngördürücü faktörü olarak mühürlenmiştir (HR = 2,46; %95 GA: 1,24–4,87; p = 0,010).

Sonuç: Mide kanserli hastalarda tanı anında BT görüntüleme ile sarkopeninin tanımlanması, genel sağkalım oranları ile ilişkilidir ve kötü prognoz için bir belirteç görevi görür.

Anahtar Kelimeler: sarkopeni, mide kanseri, sağkalım

Introduction

Gastric cancer is a common malignancy with considerable global mortality rates [1]. According to GLOBOCAN 2022 data, gastric cancer is the fifth most common cancer and the fourth largest cause of cancer-related deaths [2]. Despite recent advancements in early detection strategies and surgical techniques, a significant proportion of patients are detected with advanced disease, which has a negative impact on the prognosis [3]. In the majority of cases, the fact that the disease is diagnosed at an advanced stage is a significant factor that has a detrimental effect on the prognosis [4]. Patient characteristics are believed to influence perioperative mortality and morbidity, despite ongoing advancements in surgical procedures and cancer treatment modalities for gastric cancer [5].

Recent research emphasizes the impact of body composition, specifically skeletal muscle mass, on the clinical outcomes of cancer patients [6]. The progressive loss of skeletal muscle mass and function that is known as sarcopenia has been determined to be a serious medical condition that is related to the prognosis of cancer. It is affected by factors such as inflammation, malnutrition, tumour metabolism, and the treatment-related adverse effects. The development of cancer-associated sarcopenia is linked to several factors: anorexia, the hypermetabolic effects of the tumor, increased systemic inflammation, and gastrointestinal tract dysfunction [7]. Gastric cancer is associated with several issues such as loss of appetite, early satiety, obstruction of the gastric outlet, and malabsorption, which can lead to rapid and severe muscle loss [8]. Sarcopenia is commonly detected in patients with gastric cancer, particularly at the time of diagnosis [9]. Muscle mass is crucial for effective body composition and metabolism.

In recent years, studies on various types of cancer have shown that sarcopenia has a significant effect on prognosis [10]. Assessing sarcopenia at gastric cancer diagnosis is crucial for effective patient management. Studies employing computed CT imaging to evaluate muscle mass have found that sarcopenia at the time of diagnosis is related with poor survival [11]. Evaluating the impact of sarcopenia at diagnosis is essential for understanding disease progression, assessing mortality rates, and surgical complications. This assessment aids in identifying high-risk individuals and developing personalized therapy options for improved clinical outcomes.

This study investigates the occurrence of sarcopenia among patients diagnosed with gastric cancer who are undergoing surgery. It examines the correlation between sarcopenia and various clinical and pathological characteristics, as well as its impact on survival outcomes for these patients. This study aims to clarify the significance of sarcopenia in the management of gastric cancer, with an emphasis on enhancing clinical decision-making processes. By elucidating the implications of sarcopenia, the research seeks to improve treatment strategies and patient outcomes in individuals diagnosed with gastric cancer.

Material and Methods

This research was conducted as a retrospective analysis at a single institution. We conducted a retrospective analysis of patients who underwent surgical intervention for stomach cancer from August 2013 to February 2017. All specific information, including patient information, gender, age, Eastern Cooperative Oncology Group performance status score (ECOG PS), complete blood count, and pathological characteristics, were obtained from medical records. Patients selected for this study were required to have a confirmed diagnosis of gastric adenocarcinoma based on pathological evidence. The inclusion criteria specified that the cancer must not have invaded adjacent organs nor exhibited distant metastases. Additionally, all patients underwent surgical procedures characterized as R0 resection, which indicates that no residual tumor was left post-operation. Furthermore, the lymph node dissection performed on these patients was categorized as D1, D1+, or D2, reflecting the extent of lymph node removal associated with the surgical approach. The patients involved in the study did not have any previous history of undergoing radiotherapy or chemotherapy treatments. Additionally, there were no other medical conditions present that would have impacted the assessment of their nutritional status This research was performed in compliance with the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of Van Yuzuncu Yil University, Medical Faculty, Non-Interventional Clinical Studies, on December 21, 2018, decision number 11.

Evaluation of sarcopenia via muscle mass measurement on computed tomography scans

The muscle masses of patients diagnosed with gastric cancer were assessed using computed tomography (CT) scans conducted for staging purposes. The tomographic images of the study participants were assessed by a radiologist without prior knowledge of the patients. Patients were classified into the sarcopenia group or the non-sarcopenia group based on their skeletal muscle index, which was determined using abdomen computed tomography images. The third lumbar spinal column (L3) is the region of the body where the strongest correlation between total muscle mass and skeletal muscle mass has been observed(12). Commercial software (Terarecon version 3.4.2.11, San Mateo, CA) was utilised to quantify skeletal muscle mass. The L3 vertebra was located on axial CT, and bilateral manual delineation of the posterior paravertebral muscles was conducted. On the L3 vertebral segment, we evaluated the areas of posterior paravertebral muscles and their lean mass using a standard range of -25 to 150 Hounsfield units (HU) for skeletal muscle mass. Sarcopenia was quantified using the third lumbar skeletal muscle index (L3SMI), calculated by normalizing the muscle cross-sectional area to the square of the patient's height. This measurement is referred to as the third lumbar vertebra skeletal muscle index (L3SMI). Research indicates that L3SMI is positively correlated with the survival rates across multiple types of cancer, suggesting its potential use as a prognostic biomarker in oncology(13).

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows, version 27 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was examined by the Kolmogorov–Smirnov and Shapiro–Wilk tests. Variables with normal distributions were reported as mean ± standard deviation, whereas non-normally distributed variables were summarized as median (minimum–maximum).The prognostic performance of sarcopenia in gastric cancer was assessed using receiver operating characteristic (ROC) curve analysis, and the optimal cut-off value was identified through the Youden index. Associations between sarcopenia and demographic or clinicopathological parameters were analyzed using the chi-square test or Fisher's exact test where appropriate. Overall survival was evaluated with the Kaplan–Meier method, and the impact of sarcopenia on survival was investigated using univariate and multivariate Cox proportional hazards regression models. A two-tailed p-value < 0.05 was considered indicative of statistical significance.

Results

The median age of the 84 patients included in the study was 59 years (range, 24–80). Of these, 56% were younger than 60 years and 64.3% were male. Based on BMI distribution, approximately two-thirds of the patients were within the normal weight range, while the underweight and obese groups constituted 9.5% and 7.1% of the cohort, respectively. An ECOG performance status of 0–1 was observed in 84.5% of patients. The most common tumor locations were the corpus (38.1%), antrum (26.2%), and cardia (26.2%). Intermediate histological grade predominated, observed in 59.5% of cases. Lymphatic, vascular, and perineural invasion were present at high frequencies, each occurring in approximately 67–69% of patients. Regarding pathological staging, pT3–T4 tumors accounted for 85.7% of the cohort, and 56% of the patients were classified as stage III (Table 1).

Table 1. Baseline demographic and clinicopathological characteristics of the study cohort

Variable	Category	n (%)
Age	< 60	47 (56.0)
	≥ 60	37 (44.0)
Sex	Male	54 (64.3)
	Female	30 (35.7)
BMI	Overweight	14 (16.7)
	Normal	56 (66.7)
	Obese	6 (7.1)
	Underweight	8 (9.5)
ECOG PS	0–1	71 (84.5)
	2	13 (15.5)
Tumor location	Antrum	22 (26.2)
	Cardia	22 (26.2)
	Corpus	32 (38.1)
	Gastroesophageal junction	8 (9.5)
Histological grade	Well	8 (9.5)
	Moderate	50 (59.5)
	Poor	26 (31.0)
Lymphatic invasion	Present	57 (67.9)
	Absent	27 (32.1)
Vascular invasion	Present	58 (69.0)
	Absent	26 (31.0)
Perineural invasion	Present	56 (66.7)
	Absent	28 (33.3)
pT stage	T1–T2	12 (14.3)
	T3–T4	72 (85.7)
N stage	N0	23 (27.4)
	N1	23 (27.4)
	N2	13 (15.5)
	N3	25 (29.8)
TNM Stage	I	11 (13.1)
	II	26 (31.0)
	III	47 (56.0)

According to the ROC analysis, the predictive performance of sarcopenia for mortality was statistically significant (AUC = 0.694; p = 0.012) (Figure 1). An area under the curve of 69.4% indicates a moderately strong discriminative ability of the model in identifying mortality risk associated with sarcopenia. The 95% confidence interval ranged from 0.566 to 0.822. For the optimal cut-off value of 24.97, sensitivity and specificity were calculated as 75.8% and 61.1%, respectively (Table 2). Among all patients, 67.9% (n = 57) had sarcopenia, while 32.1% (n = 27) did not.

The association between sarcopenia and age was statistically significant (p = 0.015): the non-sarcopenic group predominantly consisted of individuals older than 60 years, whereas patients with sarcopenia were mostly younger than 60 years (64.9%). A significant difference was also observed with respect to sex (p < 0.001), as 78.9% of sarcopenic patients were male, and the prevalence of sarcopenia among females was considerably lower (21.1%). No significant difference in BMI distribution was detected between groups (p = 0.413), although the proportion of overweight individuals was slightly higher in the sarcopenia group. Regarding performance status, patients with sarcopenia demonstrated better functional capacity, with an ECOG score of 0–1 in 93% of cases compared with 66.7% in the non-sarcopenic group (p = 0.003). Tumor location, histological grade, lymphatic and vascular invasion showed no significant differences between the groups (all p > 0.05). Notably, perineural invasion occurred at the same frequency in both groups (66.7%), indicating no association (p = 0.594). Similarly, no significant difference was detected in N-stage distribution (p = 0.715), although the sarcopenia group exhibited a higher proportion of N3 disease (35.1%). Staging analysis (p = 0.461) revealed that Stage III was the most prevalent classification in both groups (55.6% in non-sarcopenia vs. 56.1% in sarcopenia) (Table 3).

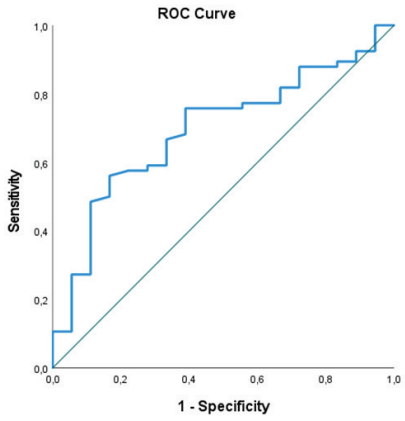

Figure 1. Receiver operating characteristic (ROC) curve for the predictive performance of sarcopenia on mortality

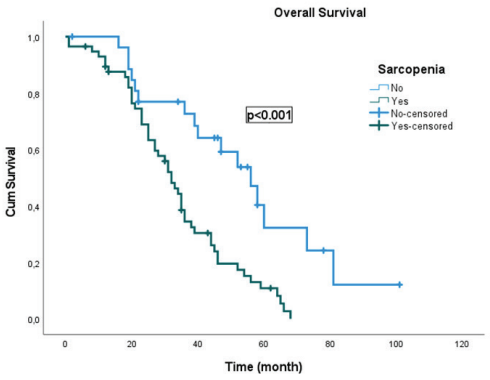

Figure 2. Kaplan–Meier overall survival curves according to the presence of sarcopenia.

Table 2. ROC analysis results for the prognostic performance of sarcopenia

AUC	Std. Errora	p	Asymptotic 95% Confidence Interval		Sensitivity	Spesiftiy	Cut off
			Lower Bound	Upper Bound			
0,694	0,065	0,012	0,566	0,822	75.8%	61.1%	24.97

Table 3. Comparison of clinicopathological characteristics according to the presence of sarcopenia

Variable	Category	No Sarcopenia n (%)	Sarcopenia n (%)	p-value
Age	< 60	10 (37.0)	37 (64.9)	
	≥ 60	17 (63.0)	20 (35.1)	**0.015**
Sex	Male	9 (33.3)	45 (78.9)	
	Female	18 (66.7)	12 (21.1)	**<0.001**
BMI	Overweight	3 (11.1)	11 (19.3)	
	Normal	17 (63.0)	39 (68.4)	
	Obese	3 (11.1)	3 (5.3)	
	Underweight	4 (14.8)	4 (7.0)	0.413
ECOG PS	0–1	18 (66.7)	53 (93.0)	
	2	9 (33.3)	4 (7.0)	**0.003**
Tumor location	Antrum	8 (29.6)	14 (24.6)	
	Cardia	8 (29.6)	14 (24.6)	
	Corpus	8 (29.6)	24 (42.1)	
	Gastroesophageal junction	3 (11.1)	5 (8.8)	0.570
Histological grade	Well	3 (11.1)	5 (8.8)	
	Moderate	17 (63.0)	33 (57.9)	
	Poor	7 (25.9)	19 (33.3)	0.489
Lymphatic invasion	Present	16 (59.3)	41 (71.9)	
	Absent	11 (40.7)	16 (28.1)	0.181
Vascular invasion	Present	16 (59.3)	42 (73.7)	
	Absent	11 (40.7)	15 (26.3)	0.140
Perineural invasion	Present	18 (66.7)	38 (66.7)	
	Absent	9 (33.3)	19 (33.3)	0.594
pT stage	T1–T2	2 (7.4)	10 (17.5)	
	T3–T4	25 (92.6)	47 (82.5)	0.184
N stage	N0	5 (18.5)	18 (31.6)	
	N1	11 (40.7)	12 (21.1)	
	N2	6 (22.2)	7 (12.3)	
	N3	5 (18.5)	20 (35.1)	0.715
Stage	I	2 (7.4)	9 (15.8)	
	II	10 (37.0)	16 (28.1)	
	III	15 (55.6)	32 (56.1)	0.461

During a median follow-up of 48.6 months, 18 patients (21.4%) died. The median overall survival for the entire cohort was 36 months (95% CI: 31.1–40.9). Median survival was substantially longer in the non-sarcopenic group, reaching 56 months (95% CI: 43.2–68.8), whereas it declined to 32 months (95% CI: 27.4–36.6) in patients with sarcopenia. This difference was highly statistically significant ($p < 0.001$). Sarcopenia demonstrated a strong and statistically significant impact on overall survival (HR = 2.83; 95% CI: 1.55–5.18; $p = 0.001$) (Figure 2). This finding indicates that the risk of mortality was nearly threefold higher in patients with sarcopenia. Sex was also identified as a significant variable in the univariate model (HR = 0.49; $p = 0.013$), suggesting that male sex was associated with greater mortality risk. In contrast, classical prognostic parameters such as age, BMI, tumor location, histological grade, as well as lymphatic, vascular, and perineural invasion—did not demonstrate significant associations in univariate analysis (all $p > 0.05$).The multivariate Cox regression analysis confirmed sarcopenia as an independent prognostic factor affecting survival (HR = 2.46; 95% CI: 1.24–4.87; $p = 0.010$). Conversely, sex did not remain significant in the multivariate model ($p = 0.398$) (Table 4).

Table 4. Univariate and multivariate Cox regression analyses for overall survival

Variable	Univariate HR	95% CI	p-value	Multivariate HR	95% CI	p-value
Age	0.799	0.488–1.310	0.374	–	–	–
Sex	0.489	0.279–0.858	0.013	0.761	0.404–1.433	0.398
ECOG PS	1.028	0.505–2.095	0.938	–	–	–
Tumor location	1.036	0.808–1.328	0.782	–	–	–
Histological grade	1.210	0.814–1.799	0.346	–	–	–
Lymphatic invasion	0.764	0.449–1.301	0.321	–	–	–
Vascular invasion	0.877	0.522–1.474	0.621	–	–	–
Perineural invasion	1.359	0.823–2.243	0.230	–	–	–
pT stage	0.919	0.489–1.728	0.794	–	–	–
N stage	1.119	0.896–1.397	0.323	–	–	–
TNM stage	1.112	0.790–1.567	0.543	–	–	–
Sarcopenia	2.831	1.548–5.178	0.001	2.460	1.243–4.869	0.010

Discussion

This study evaluated the prognostic impact of sarcopenia in patients with gastric cancer who underwent surgery. The findings of our study indicate that sarcopenia adversely affects survival rates and serves as an independent prognostic marker for patients, highlighting its significance in clinical evaluations and consideration during treatment planning. The study results are consistent with the literature demonstrating that muscle mass loss in gastrointestinal malignancies is closely related to tumor biology and the patient's systemic status [14]. Sarcopenia shows strong predictive performance for mortality, with an AUC value of 0.694 in ROC analysis. A cut-off of 24.97 was established using the Youden index, delivering a balance of sensitivity at 75.8% and specificity at 61.1%, making it clinically applicable. Previous studies also reported a significant link between sarcopenia and survival, with moderate AUC values consistently observed [15]. This indicates that sarcopenia may serve as a more effective prognostic predictor when evaluated alongside other clinical indicators, rather than in isolation.

Sarcopenia, the age-related loss of muscle mass, is found to be more prevalent in men. Research indicates that as they age, males experience a more significant decline in muscle mass compared to females and demonstrate heightened sensitivity to inflammatory responses, which could make the disease worse [16]. Men are also more likely to get more severe types of gastric cancer, which may also play a role in the development of sarcopenia [17]. In the univariate study, the sex variable was linked to death, but in the multivariate model, it became less important. This finding shows that sarcopenia plays a big role in the relationship between sex and death. The interdependent relationship between sarcopenia and age is significant [18]. This study found that sarcopenia was more prevalent in people under 60 years of age. The literature indicates a greater occurrence of sarcopenia among the elderly; nonetheless, aggressive tumour behaviour and swift metabolic decline may induce sarcopenia in younger patients, particularly in malignancies that expedite catabolic processes, such as gastric cancer [19].

This finding supports the opinion that sarcopenia is not solely an age-related occurrence but a critical indicator of tumor-associated systemic inflammation. The fact that the sarcopenia group did better on the ECOG test is an interesting result. So, this means that even in people who have surgery and are performing well at first, catabolic processes can quickly reduce their muscle mass. There are also studies that say sarcopenia can have a slow and steady progression, even in people who seem to be doing well in other areas of their lives [20]. So, it's important for routine evaluations to include objective measurements of muscles as well as performance state. Sarcopenia did not correlate with aggressive tumour characteristics such lymphatic, vascular, and perineural invasion. However, the greater N3 ratio in the sarcopenia group indicates that muscle loss may be linked to advanced nodal illness. The small sample size could explain why there is no statistical significance. It is critical to re-evaluate this relationship in larger cohorts.

The study's most important conclusion is that sarcopenia is a powerful predictor of poor survival in both multivariate and univariate analyses. The approximately 2.5–3-fold increased risk of death in patients with sarcopenia supports the hypothesis that decreased muscle mass is a systemic indicator of frailty independent of tumor behavior [21]. Perioperative difficulties, diminished chemotherapeutic tolerance, and heightened inflammatory burden highlight the correlation between sarcopenia and adverse prognosis.

Limitations of the Study

This study has some limitations. First, the relatively limited number of patients may have prevented some associations from reaching statistical significance. The single-center and retrospective design restricts the generalisability of the findings. Furthermore, thorough data on adjuvant chemotherapy, treatment tolerance, dose adjustments, treatment-related toxicity, and other therapy-related oncological outcomes were not available. As a result, it was impossible to assess the relationship between sarcopenia and treatment-related characteristics such lower chemotherapy tolerance or early treatment discontinuation. The absence of these indicators makes it difficult to evaluate whether sarcopenia has a direct impact on oncological outcomes or has an indirect effect through decreased treatment delivery. Future prospective studies incorporating comprehensive treatment and toxicity data are warranted to clarify these relationships. This study is one of the few that comprehensively examines sarcopenia in operated gastric cancer patients, including both diagnostic and prognostic aspects.

In conclusion, our study shows that sarcopenia is a substantial and independent predictor of death in gastric cancer patients. Incorporating sarcopenia assessment into clinical practice may improve risk stratification and aid in the development of more personalised treatment options, particularly in high-risk patients.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by the Ethics Committee of Van Yuzuncu Yil University, Medical Faculty, Non-Interventional Clinical Studies, on December 21, 2018, decision number 11.

Author's contributions

NÖK, MÖ, and OT designed the study. NÖK and MÖ collected the data. NÖK analyzed and interpreted the data. MÖ and OT contributed to the writing of the manuscript.

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